Book Reviews

Ciba Foundation Symposium, Vol. 179, The Molecular Basis of Smell and Taste Transduction; from a symposium, Edited by D. Chadwick, J. Marsh and J. Goode, Wiley and Sons; Chichester, 1993; ix + 287 pages. £45.00. ISBN 0471-93946-3.

This Ciba Foundation Symposium volume follows the pattern of the series in presenting not only the papers presented at the meeting, but also the often more interesting resulting discussions. This meeting and volume are especially timely in that the development of single channel recording and molecular techniques in the last decade has produced an explosion of information on the mechanisms underlying chemosensory transduction. This work centers not only on the molecular and genetic issues revolving around transduction itself, but also the intriguing question of how potential chemical stimuli in the environment gain access to the site of transduction when the sensory cells are covered by mucus or other fluid layers. This volume presents interesting glimpses into the current state of research in the area and should be of interest to those studying transduction in other biological systems as well as to other researchers in the field of chemical senses.

The molecular biology of olfactory receptors is explored in four chapters spread within the first half of the volume. Dr. Linda Buck reviews her work, with R. Axel, on the multigene family of presumed odorant receptor genes cloned from various rodents. These presomed odorant receptor genes were identified on the basis of their being structurally similar to seven-transmembrane G protein-coupled receptors in other systems, yet being unique to the olfactory receptor cells. A later chapter by D. Lancet and co-workers describes the genomic structure and organization of the putative olfactory receptor genes within their site of residence on human chromosome 17. The discussion of these and subsequent papers points out that despite much presumptive evidence that the Buck and Axel seven-transmembrane putative odorant receptors are responsible for olfactory transduction, virtually no functional studies have confirmed this claim. The possibility is raised that some olfactory receptors may be direct ligand-gated ion channels, and therefore not included in the Buck and Axel seven-transmembrane class.

Regulation of unique olfactory receptor cell genes is explored in the papers by F.L. Margolis et al. and M. Wang and R. Reed. Over three decades have passed since F. Margolis' original description of olfactory marker protein (OMP), a cytoplasmic protein nearly unique to olfactory receptor cells. Although OMP represents a sizeable percentage of the total protein in a receptor cell, and despite elucidation of its primary structure, the function of OMP remains enigmatic. Recent advances in molecular techniques have permitted identification of a putative transcription factor, olf-1, responsible for the regulation of this olfactory-specific protein. The possible role of olf-1 in regulating the restricted patterns of expression of putative odorant receptors is discussed.

Prereceptor events are summarized in the chapter by T. Getchell and co-workers. A problem for any chemosensory system is how a potential stimulus molecule gains access to the receptor cell. In the case of olfaction, an air-borne molecule must traverse a mucus barrier to reach the cilia of an olfactory receptor neuron. This chapter discusses the composition of mucus and how proteins within the mucus layer may play a role in odorant conveyance or clearance. A parallel chapter by Schmale et al. in the latter half of the book describes the potential role of salivary proteins in taste.

Olfactory receptor second messenger systems and their subsequent effect on membrane potentials are discussed respectively in chapters by Breer and by Firestein and Zufall. The discussions relate these findings to a central theme of whether an olfactory receptor cell expresses one or more than one putative olfactory receptor molecule. An interesting chapter by M. Lerner and co-workers describes a melanophore-based system for investigating G protein-coupled receptors. But as of the date of the meeting, this system had not been used successfully to study the Buck and Axel presumed odorant receptors.

Two chapters, by Carlson, Sengupta and colleagues, describe progress in the genetics of olfaction in invertebrates. While these chapters are definitely worthwhile, a curious omission from both the text and discussion is the point that the so-called olfactory system of these invertebrates does not have phyletic continuity with the olfactory system of vertebrates. Thus, these invertebrate systems may provide interesting information about how chemosensory transduction occurs in these animals, but the findings may not be generalizable to olfaction in the vertebrate lineage. Of course the power of the invertebrate systems, *Drosophila* and *Caenorhabditis*, lies in the limited number of neurons in the system and in the possibility of correlating genetic defects with specific behavioral changes.

The final section of this volume centers on taste, ranging from perireceptor events through the details of ionic flow through the gustatory epithelium. Taste receptor cells rely on diverse mechanisms to accomplish transduction including, direct interaction of taste stimuli with ion channels, ligand-gated channels and second messenger systems. Dr. S. Kinnamon describes how sour, or salivary proton concentration, is detected via two different ion channels in different species. Dr. S. McLaughlin and co-workers present data on two G proteins, transducin and gustducin, involved presumably in transduction of bitter taste. In the third chapter dealing directly with taste transduction, J. DeSimone et al. describe how sodium conductance of the entire lingual epithelium, not just the taste receptor cells, is important in understanding transduction of sodium salt taste. In the final chapter on taste, L. Bartoshuk demonstrates how the chemosensory component and tactile sensation are combined in our perception of taste. Further, she relates how taste thresholds and perception can have genetic and morphological correlates.

Overall, this succinct book presents insights into the substantial progress made in our understanding of chemosensory transduction. Readers will appreciate not only the concise overviews presented in each chapter, but should appreciate the feeling of participation offered by the interesting discussions.

Thomas E. Finger

Conjugation–deconjugation Reactions in Drug Metabolism and Toxicity. Handbook of Experimental Pharmacology, Vol. 112; Edited by F.C. Kauffman, Springer-Verlag; Berlin, Heidelberg, 1994; x + 530 pages. DM 486.00. ISBN 3-540-571221-1.

This book provides a modern and integrated overview on the main enzymes and metabolic pathways involved in phase II biotransformation of the highly reactive products formed under the catalysis of Cytochrome P450 mono-oxygenases in phase I reactions. The importance of transferases and hydrolases in the activation of drugs or carcinogens is stressed, in contrast to the more commonly

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known function of these enzymes in the detoxification processes. Despite the multiplicity of the conjugation–deconjugation enzymes, the interdisciplinarity of the subject, and the fast evolution of concepts in recent years, mainly from the molecular biology approaches, the Editor managed to provide a wholesome review and to avoid overlappings. The chapters, in a total of 17, are contributed by a remarkable board of selected authors who have themselves made inportant contributions in each specific area.

The Volume is organised in 3 Sections, respectively on the Genetic Polymorphysm and Regulation of Expression of Phase II Enzymes, on the Conjugation–Deconjugation Reactions Regulation in Intact Cells and Tissues and on the Pharmacology and Toxicology of Drug Conjugates.

Section I concerns the molecular biology of different phase II enzymes. Chapters on transferases include UDPG-T multigene family by D.J. Clarke and B. Burch, who demonstrate the importance of the major detoxification pathway catalysed by these enzymes by presenting a condensed review on their genetic identity and physiological role versus tissue-distribution. Ontogenic dependent expression and xenobiotic induction of this enzyme multigene family as well as the known genetic deficiencies and related pathologies are shortly and concisely reviewed. Most recent data on the diversity, properties and regulation of Sulfotransferase Enzymes are reviewed by R. Weinshilboum amd D. Otterness. The importance of sulfotransferases for the determination of xenobiotics, hormones and neurotransmitters net concentrations in the cells is discussed from convergent perspectives based on recent research in pharmacology, endocrinology and molecular biology. The regulation of Expression of Rat Liver Glutathione S-transferase is presented in a chapter by T.H. Rushmore, C.B. Picket and A.Y.H. Lu, as an exhaustive and elegant review on the elucidation of the structure including very recent data on the crystal structure of the GST, and on the regulation of this gene family, namely on the transcription regulation of Pi and alpha subunit genes in reponses to planar aromatic compounds and phenolic antioxidants. Human N- Acetyltransferases constitute the next chapter by K.P. Vatsis and W.W. Weber, who discuss the role of NAT1 and NAT2 genotypes in acethylation polymorphism and individual susceptibility to chemically induced disorders, a subject of utmost actuality interesting oncologists, neurologists and molecular biologists.

Deconjugation enzymes and catalysed reactions are reviewed in the following chapters which start with an interesting work on the genetic regulation and subcellular localisation of Glucuronidases by R.T. Swank, E.K. Novak and L. Zhen. This review is focused on recent work on the topogenesis mechanisms determining the native interactions of these enzymes with the endoplasmic reticulum membranes, as well as on the glucuronidase gene expression and hormone regulation. Deacylation is an important biological reaction affecting carcinogenicity and chemotherapeutic toxicity by amides. Microsomal Amidases and Carboxylesterases are reviewed by C.Y. Wang in a condensed chapter describing the recent advances in this complex area. A critical review on methyl transfer, one of the most common phase II conjugation reactions, is presented in a chapter on O-, N- and S-Methyltransferases by C.R. Creveling and D.R. Thakken, who demonstrate the pivotal role played by these enzymes in numerous physiological and metabolic functions in man.

Section II deals with factors that determine the metabolic efficiency of conjugation–deconjugation reactions in the intact cells and tissues, which therefore are essential for the physiological and pharmacological actions of drugs and endobiotic substrates. A chapter on Cofactor Supply as a Rate-Limiting Determinant of Hepatic Conjugation Reactions is written by L.A. Reinke, F.C. Kauffman and R.G. Thurman. This is a particularly well referenced work which includes a critical description of the models used to study regulation of conjugation together with brief monographs on Glucuronidation, Sulphate and Glutathione conjugation.

The following chapters concern metabolic and pharmacokynetic factors in the regulation of the steady-state levels of conjugate metabolites in the living cell. The chapter on futile cycling of conjugates written by the editor is a review of the recent studies that illustrate the involvement of specific transferases and hydrolases, localised in the same or adjacent sub cellular compartment, in the modulation of net drug metabolite concentration in the hepatic cell. The last chapter in this Section by K.S. Pang and M. Chiba deals with the mathematical description of pharmacokinetics of drug conjugates. It presents mathematical models and a quantitative treatment of steady state conjugation and deconjugation. The aspects considered are not only the membrane barriers, zonation of enzymatic activities, and protein binding but also the futile cycling, flow and cosubstrate availability, treated in previous chapters.

The third and last Section of this volume integrates five chapters on the Pharmacology and Toxicology of Drug Conjugates. It starts with a chapter on Biologically Active Conjugates of Drug and Toxic Chemicals by F.C. Kauffman, J. Zaleski, R.G. Thurman and G.Y. Kwei describing a number of illustrative examples of phase II conjugation reactions known to play relevant roles in both the inactivation and the activation of many xenobiotics. This critical review further discusses the questions of drug interactions and potentiation of pharmacological activity of drug conjugates. The following two chapters on the Acyl Glucuronides as Chemically Reactive Intermediates by C. Fenselau, and on the role of UDG transferases in Chemical Carcinogenesis, by K.W. Bock and W. Lilienblum, are excellent complements to the previous chapter on the molecular biology of UDPG super family. They constitute exhaustive reviews on acyl glucuronides cytotoxicity and carcinogenicity, which stress the role of individual UGT isoenzymes in the transport and targeting of carcinogens. The next chapter by J.A. Miller and Y.J. Surth, on the Sulfonations in Chemical Carcinogenesis gives an extensive description of the metabolic activation of aromatic amines and several other classes of carcinogens by sulphuric aced ester metabolite generation. A chapter on Glutathione Conjugate-mediated toxicities by T.J. Monks and S.S. Lau describes the most recent advances on the mechanisms through which xenobiotic GSH conjugation can result in toxicity, rather than detoxicifaciton. Paradigmatic examples of GSH conjugation generating biologically reactive intermediates illustrate this interesting review.

This book ends with a final chapter on the Challenges and Directions for a future research by F.C. Kauffman who further contexturizes the different topics, and provides suggestions for future developments in this important area.

In conclusion this book constitutes an excellent compendium integrating the enormous progress made over the last few years in the understanding of conjugation–deconjugation enzymes and reactions, and the most recent concepts on the fundamental importance of these systems in pharmacology, toxicology, and control of homeostasis. It will provide a fundamental work of reference, which was missing so far, for all those who wish to get a complete view on the specialised yet interdisciplinary field of conjugation–deconjugation and a good perspective on related upcoming new areas of drug discovery and development. The clarity of topics presentation makes this volume accessible to researchers in neighbouring areas as well as to students, though it should become a classical fundamental handbook.

Maria Celeste Lechner

The Beginnings of Cancer in the Cell. An Interdisciplinary Approach; Edited by J. Ladik and W. Förner, Springer-Verlag; Berlin, Heidelberg, New York, 1994; vii + 194 pages. DM 78.00. ISBN 3-540-57962-1.

The Beginnings of Cancer in the Cell, by Janos Ladik and Wolfgang Förner, is labelled an interdisciplinary approach to the problem, and the advertisement on the back of the book promises application of theoretical models using approved methods from quantum theory and solid state physics in conjunction with information on the disturbance of the cell's self-regulation through oncogene activation and antioncogenes. Quite a mouthful, but potentially very interesting.

However, already after the first two chapters it is clear that this book cannot help anyone in need of information on the mechanics of the creation of a cancer cell. Why is it that 'interdisciplinary approaches' so often end up being hopelessly amateurish, naive and outdated? These